UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,666	03/12/2007	Kenneth Powell	NV2-018US	2807

959 7590 06/14/2010

LAHIVE & COCKFIELD, LLP
FLOOR 30, SUITE 3000
ONE POST OFFICE SQUARE
BOSTON, MA 02109

EXAMINER	
PIHONAK, SARAH	
ART UNIT	PAPER NUMBER
1627	
MAIL DATE	DELIVERY MODE
06/14/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,666	POWELL ET AL.	
	Examiner	Art Unit	
	SARAH PIHONAK	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *25,32,33 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,26-31,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This application, filed on 3/12/2007, is a national stage entry of PCT/GB05/01018, filed on 3/18/2005.

Priority

A claim for foreign priority to Application No. 0406282.4, filed on 3/19/2004, has previously been acknowledged.

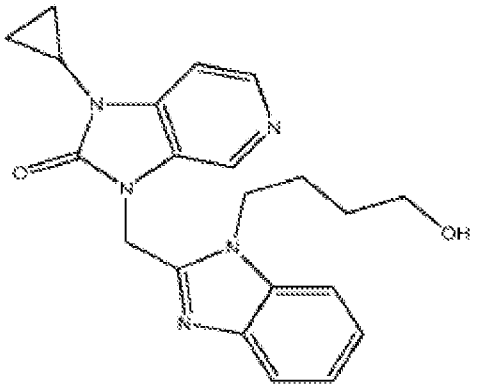
Response to Remarks

1. Applicant's arguments filed 4/5/2010, with regards to the rejection under 35 USC 103(a) have been fully considered but they are not persuasive. The Applicants have argued that the claimed invention would not have been prima facie obvious over Yu et. al., WO 2001/95910, in view of Carter et. al., WO 2004/026843, because Carter et. al. does not teach a combination of benzodiazepine with other anti-viral compounds for the treatment of RSV. The Applicants have argued that Carter et. al. teaches the combination of the benzodiazepine compound with other anti-influenza compounds, but not the combination of the benzodiazepines with anti-viral compounds. The examiner respectfully disagrees. Carter et. al. teaches the elected compound of formula (V), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, as an effective agent for inhibiting the respiratory syncytial virus (RSV). Carter et. al. also teaches that the compound can be combined with other agents for treating RSV. While the Applicants have argued that Carter et. al. explicitly teaches combination with other anti-influenza agents, it is noted that influenza is a viral infection; therefore, an anti-influenza agent would also be considered to be anti-viral. Furthermore, Carter et. al.

explicitly teaches that the elected benzodiazepine compound inhibits RSV; Yu et. al. teaches that claimed compounds of component (a) of claim (I), and of formula (I) of claim 23, also possess anti-RSV activity. As the elected benzodiazepine compound taught by Carter et. al. inhibits RSV, and the compounds of formula (I) taught by Yu et. al. also are used to treat RSV, it would have been prima facie obvious for one of ordinary skill in the art, at the time of the invention, to combine these two compounds in a pharmaceutical composition, as they are taught by the prior art to be used for the same purpose. The Applicants have argued that Carter et. al. teaches the combination of benzodiazepines with anti-influenza agents for treating concomitant RSV and influenza infections, and therefore, one of ordinary skill in the art would not have been motivated to combine the benzodiazepines with other anti-RSV compounds. This argument has not been found persuasive, as Carter et. al. explicitly teaches the elected benzodiazepine compound as being effective for inhibiting RSV. Additionally, Yu et. al. teaches that the claimed compounds of formula (I) are also effective for treating RSV. The combination of two agents which are taught by the prior art to have the same or similar utility would have been prima facie obvious, absent unexpected results. Therefore, the rejection under 35 USC 103(a) is maintained, for reasons of record. For Applicants' convenience, this rejection will be reiterated in the action below. Accordingly, this action is made **FINAL**.

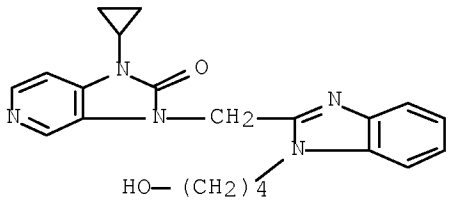
The Applicants have also asserted that the compound taught by Yu et. al. is 1-cyclopropyl-3-((1-(4-hydroxybutyl)-1H-benzo[d]imidazol-2-yl)methyl)-1H-imidazo[4,5-c]pyridin-2(3H)-one, which is shown below, and not 1-cyclopropyl-3-[1-(4-hydroxybutyl)-

1H-benzoimidazol-2-ylmethyl]-1,3-dihydro-imidazo[4,5-c]pyridine-2-one, as stated by the examiner in the office action dated 1/4/2010.



The examiner notes that the above shown compound is referred to by CAS (STN) as shown below (as the hydrochloride salt):

RN 380603-12-3 CAPLUS
CN 2H-Imidazo[4,5-c]pyridin-2-one, 1-cyclopropyl-1,3-dihydro-3-[[1-(4-hydroxybutyl)-1H-benzimidazol-2-yl]methyl]-, hydrochloride (4:5) (CA INDEX NAME)



●5/4 HCl

The compound shown above, as taught by Yu et. al., will be referred to hereafter as 1-cyclopropyl-1,3-dihydro-3-[[1-(4-hydroxybutyl)-1H-benzimidazol-2-yl]methyl]-2H-imidazo[4,5-c]pyridine-2-one.

2. Applicant's arguments, with respect to the rejection of claim 35 under 35 USC 112, first paragraph have been fully considered and are persuasive. Claim 35 has been amended to remove language drawn to "preventing"; as such, this rejection has been withdrawn.

3. Regarding the rejection of claims 1-8, 12, 16, 17, 18, 19, 23, 24, 26, 29-31, and 34 for obviousness type double patenting over claims 1-4, 7-8, 23, 24, 26, 29-31, and 34 of co-pending application No. 10/593382, the Applicants have stated that this will be addressed further when the other rejections in this application are no longer remaining. Accordingly, this rejection is maintained, for reasons of record. For convenience, this rejection will be reiterated.

4. Claims 25, 32-33, and 36-38 were previously withdrawn from consideration, due to the restriction requirement. The Applicants had previously elected 1-isopropenyl-3-(1-propyl-1H-benzoimidazol-2-ylmethyl)-1,3-dihydro-inidazo[4,5-c]pyridine-2-one as the compound for component (a) of the composition, and (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea as the compound for component (b). As stated in the office action dated 1/4/2010, the elected compound for component (a) was found to be free of the prior art. Therefore, the search was expanded to other claimed compounds for component (a), in combination with the elected compound for component (b), (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea.

5. Claims 1-24, 26-31, 34, and 35 were examined.

6. Claims 1-24, 26-31, 34, and 35 are rejected.

Claim Rejections-35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

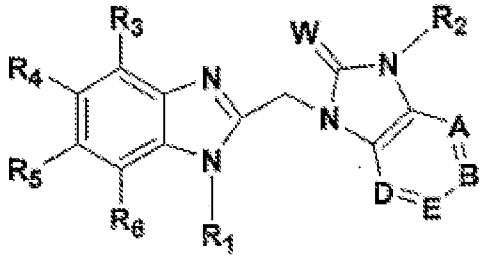
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-24, 26-31, and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et. al., WO 2001/95910 publication, in view of Carter et. al., WO 2004/026843.

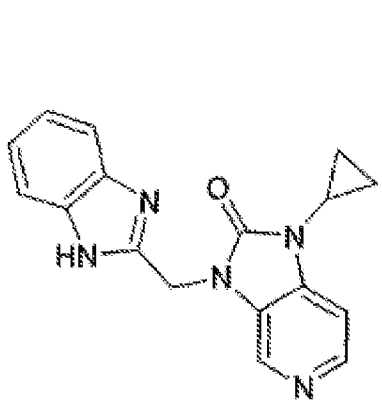
The claims are drawn to a pharmaceutical composition comprised of (a) an inhibitor of the respiratory syncytial virus (RSV) fusion protein; and (b) a benzodiazepine derivative capable of inhibiting RSV replication, in a pharmaceutically acceptable carrier or diluent. The claims are particularly directed to (a) an inhibitor of the RSV fusion protein of formula (I), and (b) a benzodiazepine derivative of formula (V).

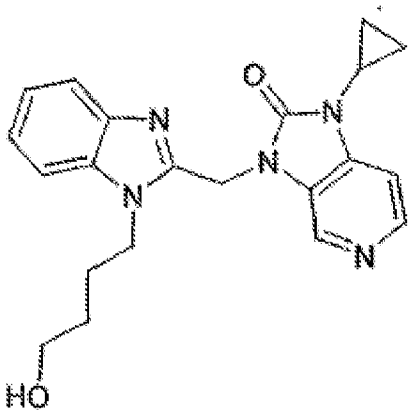
Yu et. al. teaches compounds which are effective for treatment of the respiratory syncytial virus (Abstract). Yu et. al. discloses that compounds of the formula shown below possess anti-RSV activity (p. 4, line 5-p. 7, line 6):



Where R_1=-(CR'R")$_n$-X; n=0, 1, 2, etc.; X=H, etc.; R_3, R_4, R_5, R_6=H, etc.; R_2=C_{1-12} alkenyl, C_{3-7} cycloalkyl, H, etc.; W=O, etc.; A, B, C, D=C-H, N, etc.

In particular, the compounds taught by Yu et. al. includes the species shown below, which includes 1-cyclopropyl-1,3-dihydro-3-[[1-(4-hydroxybutyl)-1H-benzimidazol-2-yl]methyl]-2H-imidazo[4,5-c]pyridine-2-one (p. 112, Example 47; p. 129, Example 73):





Additionally, Yu et. al. teaches that the cyclopropyl group of the compound shown above can be replaced by an isopropenyl, other C_{1-12} alkenyl, alkynyl, and alkyl groups (p. 4, line 5-p. 7, line 6). Yu et. al. teaches that the compounds and/or pharmaceutically acceptable salts are present in compositions with pharmaceutically acceptable carriers (p. 9, lines 10-23). Dosages between the ranges of 0.1 to 100 mg/kg body weight are also taught (p. 186, line 25-p. 187, line 5). As it is taught that the compounds inhibit the respiratory syncytial virus, it would have been expected that the RSV fusion protein associated with the virus would also have been inhibited. Treatment of mammals with the compounds is also taught (p. 9, lines 4-14).

Yu et. al. does not explicitly teach that the compounds comprise between 0.025 to 10% by weight of the composition. However, it is taught that carriers and diluents are present in the composition, along with dosage ranges. Therefore, it would have been prima facie obvious that, depending on the desired dosage and formulation, the composition would comprise between 0.025 to 10% by weight of the RSV fusion protein inhibitors.

Yu et. al. does not explicitly teach that the composition further comprises a benzodiazepine derivative capable of inhibiting RSV replication.

Carter et. al. teaches benzodiazepine derivatives in pharmaceutical compositions which are effective against the respiratory syncytial virus (Abstract). In particular, Carter et. al. discloses that the elected compound, (S)-1-(2-fluorophenyl)-3-(2-oxo-5-phenyl-2,3-dihydro-1H-benzo[e][1,4]diazepin-3-yl)urea, is effective for inhibiting the respiratory syncytial virus (p. 1, line 19-p. 2, line 20; p. 23, lines 4-5 and 8-9). Carter et. al. teaches the benzodiazepine compounds in a pharmaceutical composition with acceptable carriers (p. 37, lines 19-32), and that the composition can contain up to 85 % by weight of the claimed anti-viral compounds (p. 37, lines 22-26). It is also taught that the benzodiazepines can be combined with other anti-viral compounds for simultaneous, separate, or sequential administration (p. 36, lines 22-28). Administration of the compositions to human patients is taught (p. 35, lines 10-14).

One of ordinary skill in the art, at the time of the invention, would have been motivated to combine (a) an inhibitor of the RSV fusion protein of formula (I) as taught by Yu et. al. with (b) a benzodiazepine inhibitor of formula (V) as taught by Carter et. al. because both components (a) and (b) are taught as being effective for treating and inhibiting the respiratory syncytial virus. The combination of two or more components which are used for treatment of the same condition or for the same purpose would have been considered prima facie obvious to one of ordinary skill in the art, absent unexpected results. As the compounds taught by Yu et. al. and Carter et. al. are effective for treating the respiratory syncytial virus, one of ordinary skill in the art would

have expected success in combining these compounds together in a composition or product. As Carter et. al. teaches that the benzodiazepine compounds can be administered with other anti-viral agents either together, separately, or sequentially, it would have been prima facie obvious that the compounds taught by Yu et. al. could be combined with the compounds taught by Carter et. al. for simultaneous, separate, or sequential administration.

Claim Rejections-Obviousness Type Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-8, 12, 16, 17, 18, 19, 23, 24, 26, 29-31, and 34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 7-8, 23, 24, 26, 29-31, and 34 of copending Application No. 10/593382. Although the conflicting claims are not identical, they are not patentably

distinct from each other because both sets of claims are drawn to compositions comprised of (a) an inhibitor of the RSV fusion protein and (b) a benzodiazepine compound capable of inhibiting RSV replication. Both sets of claims are also drawn to compositions in which (a) and (b) are present in the composition at a weight percent range between 0.025-10 %.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

14. No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARAH PIHONAK whose telephone number is (571)270-7710. The examiner can normally be reached on Monday-Thursday 8:00 AM - 6:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

S.P.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1627